

(HT) from *Clostridium sordellii*, and *Clostridium novyi* α -toxin (Bette, P., et al., Toxicon 29 (1991) 877-887). Enterotoxin A and cytotoxin B have been characterized by Sullivan, N.M. et al., Infect. Immun. 35 (1982) 1032-1040, von Eichel-Streiber, C., et al., Microbiol. Pathogenesis 2 (1987) 307-318. Toxin A and toxin B are glucosyltransferases which modify threonine 37 of the GTPase Rho. By attracting of glucose at this position of Rho, this GTPase is blocked in its function. Recently, toxin B and toxin A from *C. difficile*, the causative agent of antibiotic-associated diarrhea (Lyerly, D.M., et al., Clin. Microbiol. Rev. 1 (1988) 1-18), were shown to covalently modify the mammalian protein Rho by UDP-Glc dependent glucosylation of threonine 37 (Just, I. et al., Nature 375 (1995) 500-503; Just, I., et al., J. Biol. Chem. 270 (1995) 13932-12936). Rho is a small ras related GTP-binding protein involved in the control of actin polymerization (Hall, A., Ann. Rev. Cell Biol. 10 (1994) 31-34). Glucosylation of threonine 37 of Rho by *C. difficile* toxins A or B apparently inactivates this protein and results in a loss of actin stress-fiber assembly.

At page 20, kindly replace the paragraph beginning at line 4 with the following:

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 --[To identify the acceptor amino acid glucosylated by LT, H-Ras protein as modified by LT in the presence of UDP-[¹⁴C] Glc, electrophoresed on SDS-PAGE, digested with trypsin and the resulting peptides were separated, as described in sections 1 and 2. As shown in Fig. 4A, 47 fractions were obtained. The radioactivity was exclusively associated with fractions 39 and 40 (Fig. 4A). As shown in Fig. 4B and 4C, repurification of fraction 39 or 40

gave rise to a major peptide (D for 39 and E for 40) containing the radioactivity and several other small peptides. Peptides D and E were microsequenced and gave exactly the same amino-acid sequence. Each cycle of Edman degradation was collected and counted for radioactivity. The following unambiguous sequence was found for these peptides SALTQLIQNHVDEYDPTIEDSYR (SEQ ID NO.: 5). Cycle 19 corresponding to a threonine gave a very small signal. The small amount of threonine detected in position 19 may be the consequence of the LT catalyzed glucosylation of most of Ras molecules present in the reaction. Decrease or absence of threonine 37 Rho A in automated amino-acid sequencing, after glucosylation by toxin A or B, has been already reported (Just, I. et al., Nature 375 (1995) 500-503; Just, I., et al., J. Biol. Chem.. 270 (1995) 13932-13936). The amino-acid sequence found for both peptides D and E corresponds exactly to a sequence found in the H-Ras protein between amino-acids 17 to 41 (Barbacid, M., Ann. Rev. Biochem. 56 (1987) 779-827). Radioactivity was associated first with cycle 19 and decreased thereafter (Fig. 4E). The rise in radioactivity at cycle 19 establishes threonine 35 (of the H-ras molecule) as the unique amino-acid glucosylated by LT.--

IN THE CLAIMS:

Please enter the following amended claims.

21. (Amended) An isolated A polypeptide fragment of *Clostridium sordellii* lethal Toxin (LT) with glucosyltransferase activity, consisting essentially of approximately the first 1020 N-terminal amino acids of the